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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 09 March 2000 (09.03.00)	
International application No. PCT/US99/10065	**Applicant's or agent's file reference** MSKP039WO
International filing date (day/month/year) 07 May 1999 (07.05.99)	**Priority date** (day/month/year) 08 May 1998 (08.05.98)
Applicant AGUS, David, B. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

01 December 1999 (01.12.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Juan Cruz
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

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Form PCT/IB/331 (July 1992)

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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference MSKP039WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/10065	International filing date *(day/month/year)* 07 MAY 1999	Priority date *(day/month/year)* 08 MAY 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): A01N 37/18 and US Cl.: 514/2, 12		
Applicant SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
01 DECEMBER 1999	02 OCTOBER 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer SUSAN UNGAR Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/10065

I. Basis of the report

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-12, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the claims:
pages 13-15, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the drawings:
pages 1-9, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the sequence listing part of the description:
pages 1-13, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[X] contained in the international application in printed form.

[X] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [X] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/10065

V. Reas ned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanati ns supp rting such statement

1. statement

Novelty (N)	Claims	3, 4, 7-11	YES
	Claims	1, 2, 5, 6	NO
Inventive Step (IS)	Claims	3, 4, 7-11	YES
	Claims	1-2, 5-6	NO
Industrial Applicability (IA)	Claims	1-11	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-2 lack novelty under PCT Article 33(2) as being anticipated by US Patent No. 5,550,214.

The claims are drawn to a method for active vaccination against autologous cells (B cells) expressing transmembrane proteins comprising administering a vaccine composition comprising an immunogenic portion of the extracellular domain of the transmembrane protein with a carrier protein effective to break tolerance to the transmembrane protein and a pharmaceutically acceptable adjuvant wherein the transmembrane protein is Her2-neu.

US Patent No. 5,550,214 teaches a method for active peptide vaccine wherein the immunogen is HER2/neu wherein a pharmaceutically-acceptable carrier is included (col 17, lines 60-65, wherein the carrier is a protein such as BCG, wherein an adjuvant is included and is selected from a group including Freund's complete or incomplete adjuvant (col 19, lines 51-65). It would be an inherent property of the method to vaccinate against B cells.

In the Response to PCT/IPEA/408 submitted 24 April 2000, Applicant traverses the instant objection.

Applicant argues that the cited reference peptides are not drawn to an extracellular domain and states that a copy of a summary sheet is attached. The argument has been considered but has not been found persuasive because no summary sheet has been attached and therefore could not be considered and because the '214 patent specifically states that the peptide are recognized y cancer-specific CTL's for a variety of sources (col 5) and it would be expected that this reaction would be to an extracellular epitope

Claims 1-2 and 5-6 lack novelty under PCT Article 33(2) as being anticipated by US Patent No. 5,726,023.

The claims are drawn to a method for active vaccination against autologous cells (B cells) expressing transmembrane proteins

(Continued on Supplemental Sheet.)

Supplem ntal B x
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

I. BASIS OF REPORT:

5. (Some) amendments are considered to go beyond the disclosure as filed:
NONE

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
comprising administering a vaccine composition comprising an immunogenic portion of the extracellular domain of the transmembrane protein with a carrier protein effective to break tolerance to the transmembrane protein and a pharmaceutical acceptable adjuvant wherein the transmembrane protein is Her2-neu wherein the carrier protein is KLH.

US Patent No. 5,726,023 teach a method for active vaccination against autologous cells comprising an immunogenic portion Her2-neu wherein the vaccine comprises the immunogen, Her-2/neu, and adjuvant and wherein the immunogen is coupled to KLH (col 14, lines 15-47). It would be an inherent property of the method to vaccinate against B cells.

In the Response to PCT/IPEA/408 submitted 24 April 2000, Applicant traverses the instant rejection.
Applicant argues that the '023 patent teaches the preferred use of peptides derived from amino acids 676-1255 and specifically states that the entire extracellular domain wihtout some other portions of protein is not used. The argument has been considered but has not been found persuasive because the claims are specifically drawn to a vaccine comprising at least an immunogenic portion of the extracellular domain. The cited references clearly teaches vaccines comprising peptides not only of the cytoplasmic portion but also of the extracellular domain.

Claims 3-4, 7-11 meet the criteria set out in PCT Article 33(3)-(4), because the prior art does not teach or fairly suggest a method wherein the immunogen is SEQ ID NO:1 or 2.

claims 1-11 meet the criteria set out under PCT Article 33(4).
---------- NEW CITATIONS ----------
Harlow and Lane, 1988, Antibodies a Laboratory Manuarl, Cold Spring Harbor Laboratory, Cold Spring Harbor, p. 72.

Group III

Claim 13 is generic to a plurality of distinct species which are transmembrane proteins that are different in structure and function wherein the transmembrane proteins are:

Species A - CD20 (claims 14-20)
Species B - Her2-neu (claims 14 and 18)
Species C - VEGF Receptor (claims 14 and 18)
Species D - epidermal growth factor receptor (claims 14 and 18)
Species E - CD19 ((claims 14 and 18)
Species F - interleukin-2-receptor (claims 14 and 18)
Species G - interleukin-4-receptor (claims 14 and 18)
Species H - P-glycoprotein (claims 14 and 18)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/10065

B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

GENESEQ, SWISS-PROT, SPTREMBL, APS, EMBASE, BIOSIS, MEDLINE, CAPLUS, DRUGU, PROMT, SCISEARCH, CANCERLIT, LIFESCI, TOXLINE, PHIN
search terms: vaccin?, CD20, her2, neu, erbb2

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s)1-11, drawn to a method for active vaccination against autologous cells expressing transmembrane proteins.
Group II, claim(s) 12 drawn to a method for treatment of B cell non-Hodgkin's lymphoma.
Group III, claim(s) 13-20, drawn to a vaccine composition.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking groups I-III appears to be that they all relate to a method for active vaccination with at least an immunogenic portion of the extracellular domain of a transmembrane protein.

However, Hooijberg et al (J. Immunother. Emphasis Tumor Immunol, 1996, 19(5), 346-356 specifically teaches a method of active immunization with at least an immunogenic portion of the extracellular domain of a transmembrane protein wherein that protein is CD19, wherein that protein is CD20 (see abstract).

Therefore, the technical feature linking the inventions of Groups I-III does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

The special technical feature of Group I is considered to be a method for active vaccination.

The special technical feature of Group II is considered to be a method of treatment.

The special technical feature of Group III is considered to be a vaccine composition.

Accordingly Groups I-III are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

Group I

Claim 1 is generic to a plurality of distinct species which are transmembrane proteins that are different in structure and function wherein the transmembrane proteins are:

Species A - CD20 (claims 2-11)
Species B - Her2-neu (claims 2 and 6)
Species C - VEGF Receptor (claims 2 and 6)
Species D - epidermal growth factor receptor (claims 2 and 6)
Species E - CD19 (claims 2 and 6)
Species F - interleukin-2-receptor (claims 2 and 6)
Species G - interleukin-4-receptor (claims 2 and 6)
Species H - P-glycoprotein (claims 2 and 6)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/10065

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
1-11

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/10065

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :A01N 37/18
US CL :514/2, 12
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/2, 12

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Database BIOSIS, AN 1997:22684, HOOJBERG et al. Lysis of Syngeneic Tumor B Cells by Autoreactive Cytotoxic T Lymphocytes Specific for a CD19 Antigen-Derived Synthetic Peptide. J. Immunoth. 1996, Vol. 19, No. 5, pages 346-356, see especially the Abstract.	1-11
X	US 5,550,214 A (EBERLEIN et al.) 27 August 1996, see especially cols 17-22.	1,2,5,6
X	US 5,726,023 A (CHEEVER et al.) 10 March 1998, see especially cols 3, 13, 14.	1,2,5,6

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 10 AUGUST 1999	Date of mailing of the international search report 29 SEP 1999
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer SUSAN UNGAR Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)★

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